



## Biological effects of particles from the paris subway system

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## Résumé en anglais

Particulate matter (PM) from atmospheric pollution can easily deposit in the lungs and induce recruitment of inflammatory cells, a source of inflammatory cytokines, oxidants, and matrix metalloproteases (MMPs), which are important players in lung structural homeostasis. In many large cities, the subway system is a potent source of PM emission, but little is known about the biological effects of PM from this source. We performed a comprehensive study to evaluate the biological effects of PM sampled at two sites (RER and Metro) in the Paris subway system. Murine macrophages (RAW 264.7) and C57Bl/6 mice, respectively, were exposed to 0.01-10 microg/cm<sup>2</sup> and 5-100 microg/mouse subway PM or reference materials [carbon black (CB), titanium dioxide (TiO<sub>2</sub>), or diesel exhaust particles (DEPs)]. We analyzed cell viability, production of cellular and lung proinflammatory cytokines [tumor necrosis factor alpha (TNFalpha), macrophage inflammatory protein (MIP-2), KC (the murin analog of interleukin-8), and granulocyte macrophage-colony stimulating factor (GM-CSF)], and mRNA or protein expression of MMP-2, -9, and -12 and heme oxygenase-1 (HO-1). Deferoxamine and polymixin B were used to evaluate the roles of iron and endotoxin, respectively. Noncytotoxic concentrations of subway PM (but not CB, TiO<sub>2</sub>, or DEPs) induced a time- and dose-dependent increase in TNFalpha and MIP-2 production by RAW 264.7 cells, in a manner involving, at least in part, PM iron content (34% inhibition of TNF production 8 h after stimulation of RAW 264.7 cells with 10 microg/cm<sup>2</sup> RER particles pretreated with deferoxamine). Similar increased cytokine production was transiently observed in vivo in mice and was accompanied by an increased neutrophil cellularity of bronchoalveolar lavage (84.83 +/- 0.98% of polymorphonuclear neutrophils for RER-treated mice after 24 h vs 7.33 +/- 0.99% for vehicle-treated animals). Subway PM induced an increased expression of MMP-12 and HO-1 both in vitro and in vivo. PM from the Paris subway system has transient biological effects. Further studies are needed to better understand the pathophysiological implications of these findings.

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